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ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: HUMAN ICOS LIGAND AND APPLICATION THEREOF

(57) Abstract: Human protein termed herein B7-3 encoded by the B7-3 gene has been cloned and characterised and can be made recombinantly and used. B7-3 protein is a ligand for inducible co-stimulator protein (ICOS). A soluble form of B7-3, for example comprising the extracellular domain shown to bind ICOS, is further provided, as are assay methods for obtaining agents for modulation of the interaction between B7-3 and ICOS.

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# INTERNATIONAL SEARCH REPORT

International Application No

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 C12N15/12 C12N15/11 G01N33/68 C07K16/28  
A61K38/17 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EMBL, STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! Accession number AB014553, 15 July 1998 (1998-07-15) "Homo sapiens mRNA for KIA0653 protein, partial cds." XP002156738 cited in the application the whole document	1,2,4, 17,19, 20,34, 35,38-40
X	-& ISHIKAWA K. ET AL.: "Prediction of the coding sequence of unidentified human genes. X. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro" DNA RESEARCH, vol. 5, 1998, pages 169-176, XP002089186 page 175, line 2 page 176, left-hand column, paragraph 2 --- -/--	1,2,4, 17,19, 20,34, 35, 38-40,45



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

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# INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! Accession number R23544, 23 April 1995 (1995-04-23) XP002156739 the whole document	36
X	-& HENRY J. ET AL.: "Cloning, structural analysis, and mapping of the B30 and B7 multigenic families to the major histocompatibility complex (MHC) and other chromosomal regions" IMMUNOGENETICS, vol. 46, 1997, pages 383-395, XP000971256 cited in the application page 388; figure 6 TU-D page 389, right-hand column, paragraph 5 ---	36
X	WO 99 15553 A (BUNDESREPUBLIK DEUTSCHLAND (DE); ROBERT KOCH INSTITUT (DE); KROCZEK R.) 1 April 1999 (1999-04-01) page 7, line 20-34 page 26 -page 28; claims ---	17-19, 22,23, 28,29
E	WO 00 46240 A (AMGEN INC. (US); YOSHINAGA STEVEN KIYOSHI (US)) 10 August 2000 (2000-08-10)  page 3, line 24 -page 9 page 10; figure 3 page 14; figure 12 page 19, line 33-35 page 49, line 21 -page 52, line 12 page 61, line 14 -page 64, line 13 SEQ ID NO:11,12,13,16-18 page 106 -page 111; claims ---	1,2,4-8, 11-13, 15-23, 25,28, 29,31, 34,36-45
P,X	BRODIE D. ET AL.: "LICOS, a primordial costimulatory ligand?" CURRENT BIOLOGY, vol. 10, no. 6, 10 March 2000 (2000-03-10), pages 333-336, XP000971730 page 333, right-hand column, paragraph 3 -page 334 ---	1,2,4,5, 7,8,10, 11,17, 18,21, 34-36, 38-44
P,X	LING V. ET AL.: "Identification of GL50, a novel B7-like protein that functionally binds to ICOS receptor" THE JOURNAL OF IMMUNOLOGY, vol. 164, no. 4, 15 February 2000 (2000-02-15), pages 1653-1657, XP002156735 the whole document ---	1,2,4,5, 7,8,11, 17,18, 21,34, 36,38-45
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# INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HUTLOFF A. ET AL.: "ICOS is an inducible T-cell co-stimulator structurally and functionally related to CD28" NATURE, vol. 397, 21 January 1999 (1999-01-21), pages 263-266, XP002156736 cited in the application	
A	ANGELISOVÁ P. ET AL.: "Association of the putative B-lymphocyte surface molecule B7.3 with a protein kinase activity" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 228, 1996, pages 489-493, XP002156737 abstract	1,7,8, 12,18
A	WO 95 03408 A (DANA-FARBER CANCER INST (US); REPLIGEN CORP (US); FREEMAN; NADLER ET AL) 2 February 1995 (1995-02-02) abstract page 124 -page 142; claims	
T	WANG S. ET AL.: "Costimulation of T cells by B7-H2, a B7-like molecule that binds ICOS" BLOOD, vol. 96, no. 8, 15 October 2000 (2000-10-15), pages 2808-2813, XP002156742	
T	YOSHINAGA S.K. ET AL.: "Characterization of a new human B7-related protein: B7RP-1 is the ligand to the new co-stimulatory protein ICOS" INTERNATIONAL IMMUNOLOGY, vol. 12, no. 10, October 2000 (2000-10), pages 1439-1447, XP000971269	

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.1

Although claims 22, 24-28 and 30-33 (as far as in vivo methods of treatment of the human/animal body by therapy are concerned, see pages 39-40, 44-51) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

## Continuation of Box I.2

Claims Nos.: 17 and 22-33 all in part

Present claim 17 relates to an agent defined by reference to the following desirable characteristics or properties: (1) the ability to interact with the polypeptide disclosed in present application, whose amino acid sequence is shown in SEQ ID NO:2, or with fragments thereof; (2) the ability to modulate the interaction between the polypeptide disclosed in present application (indicated as B7-3, whose amino acid sequence is shown in SEQ ID NO:2) and the polypeptide named ICOS (whose amino acid sequence is described in "Nature 1999; 397:263-266 by Hutloff et al.", cited in present application); (3) the ability to affect B7-3- or ICOS-mediated activity.

Present claims 22-33 relate in part to different uses of said agent and to methods involving said agent.

Claim 17 covers all the agents having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such agents.

In fact, present application refers in a speculative manner to proteins identified by scanning computer sequence databases (page 6), to non-peptidyl agents (page 7), to antisense molecules (pages 8-9), to ribozymes (page 9), to fragments of the B7-3 polypeptide (pages 14-15), to fragments of ICOS (page 15), to synthetic or chemical compounds (page 34), to anti-B7-3 or anti-ICOS antibodies (page 35), to mimetic compounds (pages 40-43).

However no proteins identified by scanning computer sequence databases, non-peptidyl agents, ribozymes, synthetic or chemical compounds, or mimetic compounds are disclosed in present application.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the agent by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to peptide fragments of B7-3 or ICOS, to antisense

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

molecules specific for the gene encoding B7-3 and to binding members comprising an antigen-binding domain of an antibody specific for the polypeptide of present application or specific for ICOS.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9915553 A	01-04-1999	DE 19821060 A AU 1332099 A EP 1017723 A	15-04-1999 12-04-1999 12-07-2000
WO 0046240 A	10-08-2000	AU 2859200 A	25-08-2000
WO 9503408 A	02-02-1995	US 5942607 A AU 7405294 A AU 9699198 A CA 2167091 A EP 0711345 A JP 9500788 T US 6130316 A US 6084067 A US 5861310 A	24-08-1999 20-02-1995 18-02-1999 02-02-1995 15-05-1996 28-01-1997 10-10-2000 04-07-2000 19-01-1999